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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/998,041 | 11/15/2001 | Avi J. Ashkenazi | P2730P1C34 | 4967 |
| 35489 | 7590 | 10/18/2004 | | |
| HELLER EHRLMAN WHITE & MCAULIFFE LLP 275 MIDDLEFIELD ROAD MENLO PARK, CO 94025-3506 | | | EXAMINER | |
| | | | WEGERT, SANDRA L | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1647 | |

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/998,041 | ASHKENAZI ET AL. |
| | Examiner | Art Unit |
| | Sandra Wegert | 1647 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 18 June 2004.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 119-123 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 119-123 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 15 November 2001 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date, _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>6/18/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

Detailed Action

Status of Application, Amendments, and/or Claims

Note: Applicants refer to a Declaration, submitted under 37 CFR § 1.132, in the response of 18 June 2004. However, no such Declaration has been submitted as of this date.

The Amendment and Response, submitted 18 June 2004 has been entered. Claim 119 is amended. Claim 124 is cancelled.

Claims 119-123 are under examination in the Instant Application.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

Withdrawn Objections And/or Rejections

URL's

The objection to the Specification because it contained browser-executable code, is *withdrawn*. Applicants amended the Specification to remove all URL's (18 June 2004).

35 USC § 112, first paragraph – Deposit Rules

The rejection of Claims 119-123 under 35 U.S.C. § 112, first paragraph, for not complying with the enablement requirement, is *withdrawn*. Applicants amended the Specification to insert language guaranteeing unrestricted availability of the deposited nucleic acid molecules (clone DNA59848-1512), and pointed out that the instant Specification lists the ATCC address.

35 USC § 112, second paragraph

The rejection of Claims 119-123 under 35 U.S.C. 112, second paragraph, for being indefinite is *withdrawn*. Applicants amended Claim 119 to insert the word "specifically" and cancelled Claim 124 (18 June 2004).

Maintained Objections and/or Rejections

Continuity

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119. Applicants have argued that they are entitled to the benefit of Provisional Application 60/141,037. However, since the claimed invention does not have Utility, the Provisional patent applications listed, although disclosing the same experimental assays as the instant specification, do not impart Utility to the instant invention. Therefore, the filing date of 19 November 2001 is considered as the priority date.

35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.

Claims 119-123 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under 35 U.S.C. § 101 are set forth at pp. 3-7 of the previous Office Action (18 March 2004). Claims 119-123 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (18 March 2004), one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue (18 June 2004, pp. 7-11) that the results presented in the instant Specification are enabling for the antibodies directed against the peptide of SEQ ID NO: 357. They argue that the PRO1182 nucleic acid is a diagnostic marker for breast tumors.

Applicant's arguments (18 June 2004) have been fully considered but are not found to be persuasive for the following reasons:

In the instant case, the specification provides no data that demonstrates an increase in PRO1182 DNA, RNA or protein in a tumor type. There is no evidence regarding whether or not PRO1182 mRNA or polypeptide levels are increased in cancer. Furthermore, as discussed in the previous Office Action (18 March 2004, page 13), what is often seen is a *lack* of correlation between DNA amplification and mRNA levels (Pennica, et al, 1998, Proc. Natl. Acad. Sci., 95: 14717-14722). As discussed by Haynes et al (1998, Electrophoresis, 19: 1862-1871), polypeptide levels cannot be accurately predicted from mRNA levels, and that, in their results the ratio varied from zero to 50-fold (page 1863). The literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

Further research needs to be done to determine whether or not the PRO1182 polypeptide levels increased tumor samples. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in *Brenner v. Manson*, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,

"a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the Specification's assertions that the claimed PRO1182 polypeptides have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

Conclusion

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no, however, event will the statutory period for reply expire Later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
10 October 2004

Elysa C. Kinane

ELYSIA C. KINANE
PRIVATE EXAMINER